



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : C12N 15/12, C07K 13/00 C12N 5/10, A61K 37/02 G01N 33/68		A2	(11) International Publication Number: WO 94/11502 (43) International Publication Date: 26 May 1994 (26.05.94)																																																				
(21) International Application Number: PCT/GB93/02367 (22) International Filing Date: 17 November 1993 (17.11.93) (30) Priority data: 9224057.1 ✓ 17 November 1992 (17.11.92) GB 9304677.9 ✓ 8 March 1993 (08.03.93) GB 9304680.3 ✓ 8 March 1993 (08.03.93) GB 9311047.6 ✓ 28 May 1993 (28.05.93) GB 9313763.6 ✓ 2 July 1993 (02.07.93) GB 9316099.2 ✓ 3 August 1993 (03.08.93) GB 9321344.5 ✓ 15 October 1993 (15.10.93) GB (71) Applicant (for all designated States except US): LUDWIG INSTITUTE FOR CANCER RESEARCH [GB/GB]; St. Mary's Hospital Medical School, Norfolk Place, Paddington, London W2 1PG (GB).		(72) Inventors; and (75) Inventors/Applicants (for US only): MIYAZONO, Kohei [JP/SE]; Flogstavägen 63D, S-752 63 Uppsala (SE). DIJKE, Peter, Ten [NL/SE]; Flogstavägen 25C, S-752 63 Uppsala (SE). FRANZEN, Petra [SE/SE]; Lindsbergsgatan 15b, S-752 40 Uppsala (SE). YAMASHITA, Hidetoshi [JP/SE]; Flogstavägen 33A, S-752 63 Uppsala (SE). HELDIN, Carl-Henrik [SE/SE]; Hesselmanns väg 35, S-752 63 Uppsala (SE). (74) Agent: GILL JENNINGS & EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB). (81) Designated States: AU, CA, JP, KR, NZ, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published Without international search report and to be republished upon receipt of that report.																																																					
(54) Title: ACTIVIN RECEPTOR-LIKE KINASES, PROTEINS HAVING SERINE THREONINE KINASE DOMAINS AND THEIR USE <table border="0"> <tr> <td>cons.aa</td> <td>G G G V</td> <td>A K</td> <td>Z</td> </tr> <tr> <td>MTGFBR-II</td> <td>LDTLVGKGRFAEYVIAQLKQNTSEQFETVAVKIIPPYDHYASWDRKDIIPSDINLKHENTLLOF</td> <td></td> <td></td> </tr> <tr> <td>BACTR-IIB</td> <td>LLEIKARGRFCCVWKAQLMNI-----DFVAVKI KPLQDKQSWQSEREIFSTPGQCHHEILLQF</td> <td></td> <td></td> </tr> <tr> <td>BACTR-II</td> <td>LLEVKARGRFCCVWKAQLLN-----ETVAVKIIPPIDQKQSWQNEYEVYSIPQSGGHEILLQF</td> <td></td> <td></td> </tr> <tr> <td>daf-1</td> <td>LTVRVGSGRFGNVRGDTYRG-----EAVAVKVFNAIDEPAPFKIEIEIPETRMRLRHPVRLRY</td> <td></td> <td></td> </tr> <tr> <td>subdomains</td> <td>I</td> <td>II</td> <td>III IV</td> </tr> </table> <table border="0"> <tr> <td>MTGFBR-II</td> <td>LTAERKTELKQYMLITAFHAKGHLQEYLTRHVISWEDLRNVGSSLARGLSHLKSDHTP-C</td> </tr> <tr> <td>BACTR-IIB</td> <td>IAAEGRGNSLVEVLMILITAFHDKGSLIDYLGKNIITWNLCHVAETHSRGISYLNHEDVPMCR</td> </tr> <tr> <td>BACTR-II</td> <td>IGAEKRGTSVDVDMILITAFHEKGSLSDFLKANVVSNNELCHIAETHARGLAYLHEDIPLGLK</td> </tr> <tr> <td>daf-1</td> <td>IGSDRVDVTFVTEMLVITEYHPSGSLHDFLLNTVNIETTYNLMRSTASGLAFLANQIGGSK</td> </tr> <tr> <td>subdomains</td> <td>V VI-A</td> </tr> </table> <table border="0"> <tr> <td>cons.aa</td> <td>DLK N</td> <td>DFG</td> </tr> <tr> <td>MTGFBR-II</td> <td>-GRPKPPIVHRDLKSSNIVKNDLTCCLCDPGLSLRL---CPYSSVDDLANSQQVGTARYHAP</td> <td></td> </tr> <tr> <td>BACTR-IIB</td> <td>GGGKPSIAHRDFKSNVLLKSDLTAVLADPGLAVRF---EPGKPPGD---THGQVGTTRYHAP</td> <td></td> </tr> <tr> <td>BACTR-II</td> <td>-DGHKPAISHRDIKSNVLLKQNLTACLADPGLALRF---BAGKSAGD---THGQVGTTRYHAP</td> <td></td> </tr> <tr> <td>daf-1</td> <td>-ESNKPANAHDRDIKSNVLLKQNLTAIGDLGLSLSKPEDAASDIIAN---ENYKCVTVRYLAP</td> <td></td> </tr> <tr> <td>subdomains</td> <td>VI-B</td> <td>VII VIII</td> </tr> </table>				cons.aa	G G G V	A K	Z	MTGFBR-II	LDTLVGKGRFAEYVIAQLKQNTSEQFETVAVKIIPPYDHYASWDRKDIIPSDINLKHENTLLOF			BACTR-IIB	LLEIKARGRFCCVWKAQLMNI-----DFVAVKI KPLQDKQSWQSEREIFSTPGQCHHEILLQF			BACTR-II	LLEVKARGRFCCVWKAQLLN-----ETVAVKIIPPIDQKQSWQNEYEVYSIPQSGGHEILLQF			daf-1	LTVRVGSGRFGNVRGDTYRG-----EAVAVKVFNAIDEPAPFKIEIEIPETRMRLRHPVRLRY			subdomains	I	II	III IV	MTGFBR-II	LTAERKTELKQYMLITAFHAKGHLQEYLTRHVISWEDLRNVGSSLARGLSHLKSDHTP-C	BACTR-IIB	IAAEGRGNSLVEVLMILITAFHDKGSLIDYLGKNIITWNLCHVAETHSRGISYLNHEDVPMCR	BACTR-II	IGAEKRGTSVDVDMILITAFHEKGSLSDFLKANVVSNNELCHIAETHARGLAYLHEDIPLGLK	daf-1	IGSDRVDVTFVTEMLVITEYHPSGSLHDFLLNTVNIETTYNLMRSTASGLAFLANQIGGSK	subdomains	V VI-A	cons.aa	DLK N	DFG	MTGFBR-II	-GRPKPPIVHRDLKSSNIVKNDLTCCLCDPGLSLRL---CPYSSVDDLANSQQVGTARYHAP		BACTR-IIB	GGGKPSIAHRDFKSNVLLKSDLTAVLADPGLAVRF---EPGKPPGD---THGQVGTTRYHAP		BACTR-II	-DGHKPAISHRDIKSNVLLKQNLTACLADPGLALRF---BAGKSAGD---THGQVGTTRYHAP		daf-1	-ESNKPANAHDRDIKSNVLLKQNLTAIGDLGLSLSKPEDAASDIIAN---ENYKCVTVRYLAP		subdomains	VI-B	VII VIII
cons.aa	G G G V	A K	Z																																																				
MTGFBR-II	LDTLVGKGRFAEYVIAQLKQNTSEQFETVAVKIIPPYDHYASWDRKDIIPSDINLKHENTLLOF																																																						
BACTR-IIB	LLEIKARGRFCCVWKAQLMNI-----DFVAVKI KPLQDKQSWQSEREIFSTPGQCHHEILLQF																																																						
BACTR-II	LLEVKARGRFCCVWKAQLLN-----ETVAVKIIPPIDQKQSWQNEYEVYSIPQSGGHEILLQF																																																						
daf-1	LTVRVGSGRFGNVRGDTYRG-----EAVAVKVFNAIDEPAPFKIEIEIPETRMRLRHPVRLRY																																																						
subdomains	I	II	III IV																																																				
MTGFBR-II	LTAERKTELKQYMLITAFHAKGHLQEYLTRHVISWEDLRNVGSSLARGLSHLKSDHTP-C																																																						
BACTR-IIB	IAAEGRGNSLVEVLMILITAFHDKGSLIDYLGKNIITWNLCHVAETHSRGISYLNHEDVPMCR																																																						
BACTR-II	IGAEKRGTSVDVDMILITAFHEKGSLSDFLKANVVSNNELCHIAETHARGLAYLHEDIPLGLK																																																						
daf-1	IGSDRVDVTFVTEMLVITEYHPSGSLHDFLLNTVNIETTYNLMRSTASGLAFLANQIGGSK																																																						
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MTGFBR-II	-GRPKPPIVHRDLKSSNIVKNDLTCCLCDPGLSLRL---CPYSSVDDLANSQQVGTARYHAP																																																						
BACTR-IIB	GGGKPSIAHRDFKSNVLLKSDLTAVLADPGLAVRF---EPGKPPGD---THGQVGTTRYHAP																																																						
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subdomains	VI-B	VII VIII																																																					
(57) Abstract A new receptor family has been identified, of activin-like kinases. Novel proteins have activin/TGF- β -type I receptor functionality, and have consequential diagnostic/therapeutic utility. They may have a serine/threonine kinase domain, a DFKSRN or DLKSKN sequence in subdomain VIB and/or a GTKRYM sequence in subdomain VIII.																																																							